REMARKS

The Invention

The present invention features methods and compositions useful for treating diseases associated with tissue necrosis.

Support for Amendments

Claims 9, 24, and 41 are amended in accordance with the Examiner's suggestions. The amendments to claims 9 and 41 are grammatical. The amendment to claim 24 is generally supported by the specification at page 2, lines 10-12. No new matter is introduced by these amendments.

A "marked up" version of the claims showing the changes made and an appendix of the claims as pending are attached.

The Office Action

Claims 1, 2, 9, 10, 17-25, 32-37, and 41 are pending in this application. All pending claims stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement and under 35 U.S.C. § 112, second paragraph, for indefiniteness. These rejections are addressed below, in the order in which they appear in the Office Action.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 9, 10, 17-25, 32-37, and 41 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the Examiner asserts that the specification does not enable a person of ordinary skill in the art to make the claimed derivatives of compound ID# 115807. The Examiner does, however, concede that the specification is enabling for compound ID# 115807 itself. Applicants respectfully traverse this rejection.

The Federal Circuit has repeatedly stated that

> enablement is determined from the viewpoint of persons of skill in the field of the invention at the time the patent application was filed. *Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 56 U.S.P.Q.2d 1332 (Fed. Cir. 2000).

Further, the law

> permits [the Applicant to] resort to material outside of the specification in order to satisfy the enablement portion of the statute because in makes no sense to encumber the specification of a patent with all the knowledge of the past concerning how to make and use the claimed invention. *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374 (Fed. Cir. 1999).

See, also, *Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys.*, 804 F.2d 659, 231 U.S.P.Q. 649 (Fed. Cir. 1986) "A patent applicant need not include in the specification that which is already known to and available to the public."; and *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987) "A patent need not teach, and preferably omits, what is well known in the art." Thus, the law is well settled regarding the scope of the disclosure necessary to satisfy the enablement requirement of § 112; the Applicants need only describe that which is unknown in the art and is necessary for the successful practice of the claimed invention.

Applicants respectfully submit that the synthetic methods for the Compound ID# 115807 derivatives that are the subject of the claimed methods were well known at the time of application filing. As described extensively in the accompanying Declaration of Alexei Degterev, under 37 C.F.R. § 1.132, Compound ID# 115807 and its derivatives are thiohydantoins which can be synthesized from tryptophan and/or tryptophan analogs. Specifically, Compound ID# 115807 may be synthesized using the same reaction as performed during "Edman degradation," a well known method using in protein sequencing reactions (see, for example, Edman, Acta Chem. Scand., 4: 283-293, 1950; Waterfield *et al.*, Biochemistry, 9: 832-839, 1970). Edman describes chemical reactions using methyl isothiocyanate to catalyze the formation of a thiohydantoin ring on various

amino acid structures. Hawke (U.S. Patent No. 4,837,165) describes a modified Edman reaction using dimethyl isothiocyanate which results in different substitutions of the thiohydantoin ring formed using the Edman method.

Furthermore, at the time of application filing, a large number of tryptophan analogs were known and readily available to the skilled artisan. For example, known tryptophan derivatives include, for example, 1-methyl-tryptophan (CAS 110117-83-4), 4-methyl-tryptophan (CAS 1954-45-6), 5-benzyloxy-tryptophan (CAS 6383-707-6), 5-bromo-tryptophan (CAS 6548-09-0), 5-fluoro-tryptophan (CAS 154-08-5), 5-hydroxy-tryptophan (CAS 103404-89-3), 5-methoxy-tryptophan (CAS 28052-84-8), 6-fluoro-tryptophan (CAS 7730-20-3), 6-methyl-tryptophan (CAS 2280-85-8), 7-benzyloxy-tryptophan (CAS 66866-40-8), and 7-methyl-tryptophan (CAS 17332-70-6). These, or any other appropriate tryptophan derivatives, can be substituted for tryptophan and used to create the other thiohydantoin derivatives of the present invention.

Applicants respectfully submit that a person of ordinary skill in the art knows how to make the derivatives of the claimed invention in view of the teachings of the specification and that which were known in the art at the time the application was filed. Accordingly, this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 9, 10, 17-25, 32-37, and 41 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Applicants note that claims 1 and 2 have been canceled and the remaining claims have been amended in accordance with the Examiner's suggestions. Accordingly, this rejection may be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. Enclosed is a petition to extend the period for replying for three months, to and including September 9, 2002, as September 7 and 8, 2002, fall on a Saturday and Sunday, respectively. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Applicants respectfully request that, effective immediately, all communication in this case be addressed to:

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Respectfully submitted,

Date: September 3, 2002

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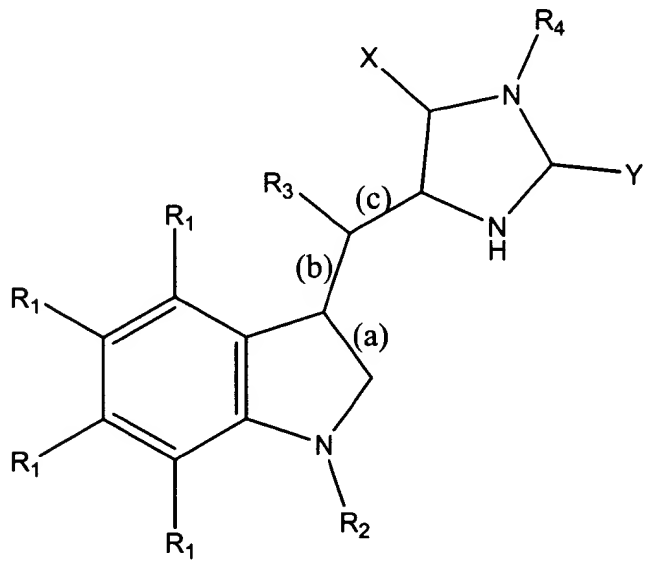
Version With Markings to Show Changes Made

9. (Twice amended) A method for decreasing necrosis, said method comprising treating a cell with a chemical compound, said compound [having] <u>of</u> the formula:



wherein

each R_1 is independently selected from the group consisting of hydrogen, methyl, carboxy, hydroxyl, methoxyl, amino, and nitro;

R_2 is selected from the group consisting of hydrogen, alkyl, and acyl;

R_3 is selected from the group consisting of alkyl, acyl, halogen, hydrogen, [or] <u>and</u> hydroxyl;

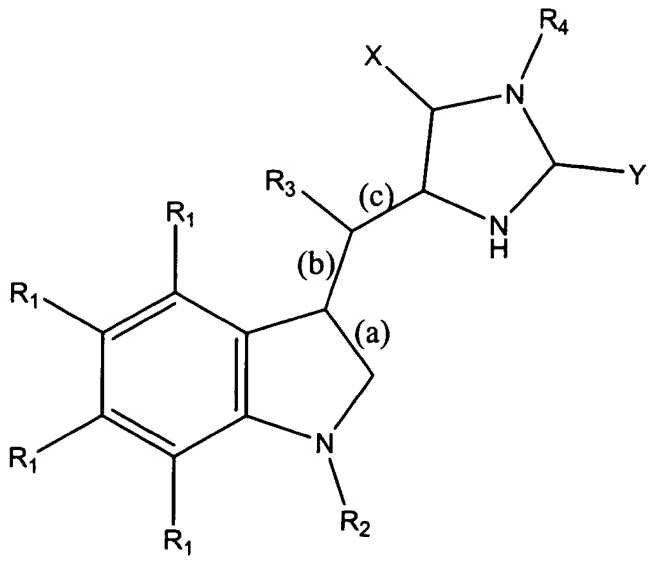
R_4 is selected from the group consisting of methyl, hydroxyl, carboxyl, and linear and branching alkyl groups;

X is selected from the group consisting of =O, -OH and -H;

Y is selected from the group consisting of =S and $-SR_5$, where R_5 is either hydrogen or an alkyl group; and

each of the bonds (a), (b), and (c) independently is either a double or single bond, provided, however, that bond (a) and bond (b) are not both double bonds.

24. (Twice amended) A method for treating a condition [characterized by necrosis,] in a patient, wherein decreasing necrosis is of benefit, said method comprising the steps of administering a chemical compound having the formula:



to said subject, in a dosage sufficient to decrease necrosis, wherein

each R_1 is independently selected from the group consisting of hydrogen, methyl, carboxy, hydroxyl, methoxyl, amino, and nitro;

R_2 is selected from the group consisting of hydrogen, alkyl, and acyl;

R_3 is selected from the group consisting of alkyl, acyl, halogen, hydrogen, [or] and hydroxyl;

R_4 is selected from the group consisting of methyl, hydroxyl, carboxyl, and linear and branching alkyl groups;

X is selected from the group consisting of =O, -OH and -H;

Y is selected from the group consisting of =S and $-SR_5$, where R_5 is either hydrogen or an alkyl group; and

each of the bonds (a), (b), and (c) independently is either a double or single bond, provided, however, that bond (a) and bond (b) are not both double bonds.

41. (Amended) The method of claim 24, wherein said condition [characterized by necrosis] is a neurodegenerative disease, stroke, liver disease, pancreatic disease, ischemic brain injury, ischemic heart injury, ischemic injury to non-cardiac and non-neural tissue, head trauma, necrotic ulceration, septic shock, coronary heart disease, gastrointestinal disease, tuberculosis, viral infection, or conditions associated with HIV infection or AIDS.